SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE
AZOMID 250 (TABLET)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains: Acetazolamide 250 mg
Contains sugar: Lactose monohydrate 150 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Tablets
White, round, normal biconvex tablet with quadrisected top, measuring 12,7 mm in diameter.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Acute primary and secondary glaucoma.

4.2 Posology and method of administration
For the treatment of glaucoma:
500 mg initially, then 250 mg every 6 to 8 hours.

Paediatric population
Safety and efficacy in children have not been established.

Method of administration
For oral use.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
Acetazolamide is contraindicated in the presence of sodium or potassium depletion, in idiopathic renal hyperchloraemic acidosis, in conditions such as Addison's disease and adrenal failure, and in marked hepatic or renal failure. It should not be used in chronic, non-congested closed angle glaucoma as the condition may deteriorate. The use of acetazolamide should be avoided in the first trimester of pregnancy (see section 4.6).
AZOMID tablets should not be used in patients hypersensitive to sulphonamides (see section 4.4).

4.4 Special warnings and precautions for use
Rarely, in patients with hepatic cirrhosis, it may cause disorientation.
Appreciable loss of sodium and potassium during prolonged therapy with acetazolamide

may result in a tendency towards hypokalaemic acidosis.
By rendering the urine alkaline, acetazolamide enhances the effect of amphetamines and reduces the effect of hexamine and its compounds; it may enhance the effect of quinidine (see section 4.5).
Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. A meta-analysis of randomized placebo controlled trials of anti-epileptic drugs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for Acetazolamide.
Therefore, patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.
When AZOMID tablets is prescribed for long-term therapy, special precautions are advisable.
The patient should be cautioned to report any unusual skin rash. Periodic blood cell counts and electrolyte levels are recommended. Fatalities have occurred, although rarely, due to severe reactions to sulphonamides (see section 4.3). A precipitous drop in formed blood cell elements or the appearance of toxic skin manifestations should call for immediate cessation of AZOMID tablets therapy.
In patients with pulmonary obstruction or emphysema where alveolar ventilation may be impaired, AZOMID tablets may aggravate acidosis and should be used with caution.

In patients with a past history of renal calculi, benefit should be balanced against the risk of precipitating further calculi.

The occurrence at the treatment initiation of a feverish generalized erythema associated with pustula may be a symptom of acute generalized exanthematous pustulosis (AGEP) (see section 4.8). In case of AGEP diagnosis, acetazolamide should be discontinued and any subsequent administration of acetazolamide contraindicated.

Contains lactose
Patients with rare hereditary problems of galactose intolerance, total lactose deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction
The diuretic effect of acetazolamide is diminished if ammonium chloride is taken concomitantly.
Acetazolamide is a sulphonamide derivative. Sulphonamides may potentiate the effects of folic acid antagonists. Possible potentiation of the effects of folic acid antagonists, hypoglycaemics and oral anti-coagulants may occur.
Concurrent administration of acetazolamide and aspirin may result in severe acidosis and increase central nervous system toxicity. Adjustment of dose may be required when AZOMID tablets is given with cardiac glycosides or hypertensive agents.
When given concomitantly, acetazolamide modifies the metabolism of phenytoin, leading to

increased serum levels of phenytoin. Severe osteomalacia has been noted in a few patients taking acetazolamide in combination with other anticonvulsants. There have been isolated reports of reduced primidone and increased carbamazepine serum levels with concurrent administration of acetazolamide.
Because of possible additive effects, concomitant use with other carbonic anhydrase inhibitors is not advisable.
By increasing the pH of renal tubular urine, acetazolamide reduces the urinary excretion of amphetamine and quinidine and so may enhance the magnitude and the duration of effect of amphetamines and enhance the effect of quinidine.
Ciclosporin: Acetazolamide may elevate ciclosporin levels.
Methenamine: Acetazolamide may prevent the urinary antiseptic effect of methenamine (see section 4.4).
Lithium: Acetazolamide increases lithium excretion and the blood lithium levels may be decreased.
Sodium bicarbonate: Acetazolamide and sodium bicarbonate used concurrently increases the risk of renal calculus formation.

4.6 Fertility, pregnancy and lactation
Pregnancy
The use of acetazolamide should be avoided in the first trimester of pregnancy (see section 4.3).

Breast-feeding
Acetazolamide has been detected in low levels in the milk of lactating who have taken Acetazolamide tablets. Although it is unlikely that this will lead to any harmful effects in the infant, extreme caution should be exercised when Acetazolamide tablets is administered to lactating women.

Fertility
Not available.

4.7 Effects on ability to drive and use machines
Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia. Less commonly, fatigue, dizziness and ataxia have been reported. Disorientation has been observed in a few patients with oedema due to hepatic cirrhosis. Such cases should be under close supervision. Transient myopia has been reported.

These conditions invariably subside upon diminution or discontinuance of the medication. If affected, the patient should not drive or use machines.

4.8 Undesirable effects

a) Summary of safety profile

During short-term therapy, you may experience the feeling of thirst, but this is usually non-serious. During long-term therapy, metabolic acidosis and electrolyte imbalance may occasionally occur. This can usually be corrected by the administration of bicarbonate. Conditions that invariably subsides upon diminution or withdrawal of the medication include transient myopia.
Acetazolamide is a sulphonamide derivative and therefore some side-effects similar to those caused by sulphonamides have occasionally been reported. These side-effects include fever, anaphylaxis, crystalluria, renal and ureteral colic, calculus formation, rash (including Erythema multiforme, Steven-Johnson syndrome, Toxic epidermal necrolysis), Fulminant hepatic necrosis and Agranulocytosis.

b) Tabulated list of adverse reactions

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTIONS
Blood and lymphatic system disorders	Frequency unknown	Agranulocytosis, Aplastic anaemia, Thrombocytosis, Leukopenia, Bone marrow depression, Pancytopenia
Metabolism and nutrition disorders	Frequency unknown	Hypokalaemia acidosis, Thirst, Metabolic acidosis, Electrolyte imbalance
Psychiatric disorders	Frequency unknown	Excitement, Depression, Irritability, Reduced libido, Occasional instances of confusion
Nervous system disorders	Frequency unknown	Drowsiness and numbness and tingling of face and extremities, Dizziness, Headache, Ataxia, Paraesthesia, Flaccid paralysis
Eye disorders	Frequency unknown	Transient myopia
Ear and labyrinth disorders	Frequency unknown	Tinnitus, Hearing loss
Respiratory, thoracic and mediastinal disorders	Frequent	Hyperpnoea
Gastrointestinal disorders	Frequency unknown	Gastrointestinal disturbances, Melaena, Taste disturbance, Nausea, Vomiting, Diarrhoea

Hepatobiliary disorders	Frequency unknown	Fulminant hepatic necrosis, Hepatitis or cholestatic jaundice
Skin and subcutaneous tissue disorders	Frequency unknown	Skin rash (including Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis), Urticaria, Thrombocytic purpura, Photosensitivity, Acute generalized exanthematous pustulosis (AGEP)
Renal and urinary disorders	Frequency unknown	Renal lesions, Haematuria, Crystalluria, Renal and ureteral colic, Renal failure, Calculus formation, Glycosuria, Polyuria
General disorders and administration site conditions	Frequency unknown	Fatigue, fever, Anaphylaxis, Flushing
Investigations	Frequency unknown	Abnormal liver function

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
None known.
No specific antidote. Supportive measures with correction of electrolyte and fluid balance. Force fluids.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
A 15.4 Ophthalmic preparations – others
Pharmacotherapeutic group: Carbonic anhydrase inhibitors.
Code: S01EC01.
Acetazolamide is an inhibitor of carbonic anhydrase. By inhibiting the reaction catalysed by carbonic anhydrase in the renal tubules, acetazolamide increases the excretion of bicarbonates and of cations, chiefly sodium and potassium, and so promotes an alkaline diuresis.
By inhibiting carbonic anhydrase in the eye, acetazolamide reduces the rate of aqueous humour formation, and thus decreases intra-ocular pressure. A mild degree of metabolic acidosis persists for as long as the medicine is given.

5.2 Pharmacokinetic properties

Absorption

Acetazolamide is fairly rapidly absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 2 hours after administration by mouth.

Distribution

It has been estimated to have a plasma half-life of about 4 hours. It is tightly bound to carbonic anhydrase and accumulates in tissues containing this enzyme, particularly red blood cells and the renal cortex. It is also bound to plasma proteins.

Elimination

It is excreted unchanged in the urine; renal clearance being enhanced in alkaline urine.

5.3 Preclinical safety data

No information available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch
Pregelatinized starch
Magnesium stearate
Preservative: Nipastat/Salistat (total parabens) 0,199 % m/m

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

White, polypropylene securitainer with LDPE (low density polyethylene) closure of 100 tablets.
White, cylindrical, screw type, HDPE (high density polyethylene) container with HDPE screw cap of 100 tablets.
Amber glass bottle with LDPE cap of 100 tablets.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road,
Erand Gardens,

Midrand, 1685
Customer Care: 0860 ADCOCK / 232625

8. REFERENCE NUMBER/S
H1805 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
December 1974

10. DATE OF REVISION OF THE TEXT
24 January 2024